October 7, 2003

John E. Heinze, Ph.D.
Manager, LAB Sulfonic Acids Coalition
The LAB Sulfonic Acids Coalition
529 14th Street N.W.
Suite 655
Washington, DC 20045

Dear Dr. Heinze:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Linear Alkylbenzene Sulfonic Acids Category posted on the ChemRTK HPV Challenge Program Web site on June 6, 2003. I commend The LAB Sulfonic Acids Coalition for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Coalition advise the Agency, within 90 days of this posting on the Web site, of any modifications to their submission. Please send any electronic revisions or comments to the following addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
R. Gonzalez
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Linear Alkylbenzene (LAB) Sulfonic Acids Category

Summary of EPA Comments

The sponsor, the Linear Alkylbenzene Sulfonic Acids Coalition, submitted a test plan and robust summaries to EPA for the Linear Alkylbenzene (LAB) Sulfonic Acids Category dated May 20, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on June 6, 2003. The category consists of C_{10-16} alkylbenzene sulfonic acids (CAS No. 68584-22-5), dodecylbenzene sulfonic acid (CAS No. 27176-87-0), and tridecylbenzene sulfonic acid (CAS No. 25496-01-9). Supporting substances include C_{10-13} alkylbenzene sulfonic acids and seven linear alkylbenzene sulfonate salts (LAS).

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The data and rationale provided adequately support the category.

2. Physicochemical Properties and Environmental Fate. The submitter needs to provide vapor pressure data for at least two of the category members and state the input values used in fugacity models in the robust summaries.

3. Health Effects. Adequate data are available for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

4. Ecological Effects. EPA reserves judgement on the adequacy of all ecological endpoints pending receipt of critical missing data elements in the robust summaries.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on the Linear Alkylbenzene (Lab) Sulfonic Acids Category Challenge Submission

General

The test plan did not discuss all of the substances for which robust summaries were submitted–for example, a C_{10}-C_{14} derivative (CAS No. 69669-44-9) that was the subject of the submitted repeated-dose oral toxicity assay.

Category Definition

The submitter proposed the linear alkylbenzene (LAB) sulfonic acids category to cover three sponsored substances containing para-*sec*-alkyl-substituted benzenesulfonic acids and eight non-sponsored substances to provide supporting data:

Chemical Name	CAS Number
C_{10-16}-alkyl derivatives of benzene sulfonic acid	68584-22-5
Dodecylbenzene sulfonic acid	27176-87-0
Tridecylbenzene sulfonic acid	25496-01-9
Decylbenzene sulfonic acid, sodium salt	1322-98-1
Dodecylbenzene sulfonic acid, sodium salt	25155-30-0
Tridecylbenzene sulfonic acid, sodium salt	26248-24-8

Undecylbenzene sulfonic acid, sodium salt	27636-75-5
mono-C_{10-16}-alkyl derivatives of benzenesulfonic acid, sodium salts	68081-81-2
C_{10-13}-alkyl derivatives of benzene sulfonic acid, sodium salts	68411-30-3
mono-C_{10-14}-alkyl derivatives of benzene sulfonic acid, sodium salts	85117-50-6
4-C_{10-13}-sec-alkyl derivatives of benzene sulfonic acid	85536-14-7

Four of the supporting substances, CAS Nos. 1322-98-1, 26248-24-8, 27636-75-5, and 68081-81-2, were listed in Table 2 of the test plan but could not be identified in the robust summaries; i.e., no data were provided on these substances. The submitter needs to reconcile the apparent discrepancy. CAS No. 85536-14-7 is referred to as European LAB sulfonic acids in the test plan and robust summaries and was added as a representative substance to fill data gaps for the sponsored substance, CAS No. 68584-22-5. The remaining seven non-sponsored substances are produced from LAB sulfonic acids by neutralization to produce the associated sodium salts.

Finally, several other linear alkylbenzene sulfonates are included in the robust summaries only to provide additional supporting data but are not listed in Table 2 of the test plan. These substances are: C_{10-14} benzene sulfonic acid, sodium salt (CAS No. 69669-44-9); alkylbenzene sulfonate, sodium salt (commercial name P-500 N-Na, no CAS No. given); and linear C_{10-13}-alkylbenzene sulfonic acid (commercial name dobanic acid, no CAS No. given). The submitter needs to list these substances in Table 2 in the test plan as well.

Category Justification

The submitter supports the LAB sulfonic acid category on the basis of the structural similarity and narrow range of alkyl chain length that will result in similar physicochemical, environmental fate, and toxicological properties of the category members. As noted above, the submitter used the sodium salts of alkylbenzene sulfonic acids (LAS) as representative of the category members because both LABs and LASs will exist in the dissociated state at environmental and physiological pHs. The submitter also noted that LAB sulfonic acids and LASs will differ for some physicochemical properties, such as melting point, boiling point, and vapor pressure, because LASs are salts, and these "are not appropriate to compare." The submitter's approach and use of LAS as representative of LAB sulfonic acids for certain endpoints are reasonable.

The LABs have low melting points and high measured water solubilities, and the single measured log K_{ow} value in the category of 2 for C_{10-16}-alkyl derivatives of benzene sulfonic acid is similar to the calculated values of 1.96 and 2.52 for CAS Nos. 25155-30-0 and 26248-24-8, respectively. Although there are some inconsistencies in the values (e.g., boiling points), other physicochemical data help support the category.

Given their similar structures, the three sponsored substances are expected to have similar fate properties. Biodegradation data are available for CAS Nos. 85536-14-7, 27176-87-0 and 68411-30-3. These data are consistent and consequently support the category.

Limited comparative health effects data were provided to support the category. Acute oral LD_{50} values were in the same range for CAS Nos. 68584-22-5 and 27176-87-0 and two analogs, CAS Nos. 68411-30-3 and 85536-14-7. CAS No. 27276-87-0 was found to be corrosive and the analog CAS No. 85536-14-7 was found to be highly irritating in skin irritation tests in guinea pigs. Bacterial mutagenicity testing was negative for CAS No. 68584-22-5 and the analog, CAS No. 68411-30-3. Similarities in other health effects are to be expected because of the narrow range of alkyl chain lengths of category members.

Although EPA is reserving judgement on the adequacy of submitted ecological data, similarities in ecological effects are expected because of the narrow range of alkyl chain lengths of category members.

Overall, the data and reasoning provided adequately support the category.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility)

The data provided by the submitter for melting point, boiling point, octanol/water partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

Table A-1does not indicate which data are measured and which are estimated. The table also does not always indicate when a surrogate material is used to satisfy the endpoint.

Melting point. The category members are mixtures and will not have well-defined melting points. The submitter provided several melting points in the range < -10 °C to 10 °C. No further testing is necessary.

Boiling point. The submitter provided boiling points of 315 and 205 °C for dodecylbenzenesulfonic acid. The submitter also provided a boiling point of 156 °C for a C10-C12 mixture. EPA estimations (MPBPWIN v1.41) for representative structures were 430, 453, and 465, respectively. While there is no clear agreement between the boiling points provided by the submitter and those found in the literature or by estimation, the category members are mixtures and will not have well defined boiling points. The estimated boiling points further suggest that the boiling points of category members would be >300 °C and that testing is thus not needed for this endpoint.

Vapor pressure. The submitter did not provide vapor pressure data for any of the category members. The submitter provided a vapor pressure of 0.22 hPa (0.17 mm Hg) (no temperature stated) for an alkylbenzene sulfonic acid that contained 18.3% of n-decylbenzenesulfonic acid (CAS No. 140-60-3), 42.1% of Undecylbenzenesulfonic acid (CAS No. 50854-94-9), and 30.0% of dodecylbenzenesulfonic acid (CAS No. 27176-87-0). The vapor pressure for this substance is questionable. If determined at 25 °C, the value is much higher than the estimated vapor pressures of the three main components, which range from 10^{-9} to 10^{-11} mm Hg at 25 °C. Therefore, the data provided by the submitter are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide vapor pressure data following OECD guidelines for at least two members of this category in order to have an accurate assessment of this endpoint. According to OECD guidelines, estimated values below 10^{-5} Pa (10^{-8} mm Hg) are acceptable.

Partition coefficient. The category members are surfactants and measurement of a log K_{ow} will be problematic. EPA agrees with the submitter that the LAB acids and their sodium salts will be completely ionized (pK_a <1) in solution at environmentally relevant pHs and comparisons between the two will be appropriate. The log K_{ow} values for sodium dodecylbenzenesulfonate (CAS No. 25155-30-0) and sodium dodecylbenzenesulfonate (CAS No. 25155-30-0) reasonably represent the category members.

Water solubility. The category members are surfactants and measurement of water solubility is problematic. Since they form micelles in water, they may be better described as dispersible rather than miscible in water. As with log K_{ow}, comparison of the sodium salts and the acids is appropriate. Although estimated values might provide reasonable theoretical water solubilities for these chemicals, EPA suggests that the submitter consider whether it is more appropriate to cite available data on critical micelle concentrations of the salts.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water, biodegradation, and transport and distribution (fugacity) are adequate for the purposes of the HPV Challenge Program.

Fugacity. The submitter needs to provide the input values used in fugacity models in the robust summaries.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for the acute toxicity endpoint for two category members (CAS Nos. 68584-22-5 and 27176-87-0) and for gene mutations for CAS No. 68411-30-3, an analog, for the purposes of the HPV Challenge Program. The data for chromosomal aberration for CAS No. 85536-14-7, an European LAB sulfonic acid, are acceptable, but the robust summary needs revision. The data submitted for the repeated-dose, reproductive and developmental toxicity endpoints for analogs, CAS No. 69669-44-9, LAS C10-C14, sodium salt (no CAS No. given), and a Japan LAS (average alkyl chain length = C11.7-12.3; no CAS No. given), were summarized from a secondary source and reviewed by the International Program on Chemical Safety (IPCS), and were accepted by the OECD SIDS Program. Therefore, these data are acceptable for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

Genetic toxicity. The test plan (p. 14) indicated that *in vivo* genotoxicity data were provided for CAS No. 68584-22-5; however, the submitted data were for CAS Nos. 85536-14-7 and 69669-44-9. The submitter needs to address this discrepancy.

Ecological Effects (fish, invertebrates, and algae)

EPA reserves judgement on the adequacy of the fish, daphnia, and algae studies pending receipt of critical missing data elements in the robust summaries (*see* Specific Comments on the Robust Summaries below).

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. A robust summary for an acute oral toxicity study on CAS No. 68584-22-5 in rats is missing the purity (or activity as stated in the robust summaries) of the test substance and a range or 95% confidence interval for the LD50. The submitter needs to clarify whether a group of three fasted females was also treated with the starting 2000 mg/kg/bw dose.

Genetic toxicity. Missing information in a robust summary for a reverse mutation assay in *Salmonella typhimurium* for the supporting compound, CAS No. 68411-30-3, includes the concentration levels (only a range was given), the number of replicates per concentration, the positive and negative controls, the source of the metabolic activation system, the number of colonies per concentration that were counted, and the criteria for positive results.

Although an *in vivo* micronucleus assay in mice treated with an analog, CAS No. 85536-14-7, was an OECD guideline study, the robust summary is missing critical information including the gavage vehicle, the number of animals tested, the concentration levels, the positive and negative controls, the time of exposure, the number of erythrocytes examined, the criteria for positive results, and the data for exposures less than 72 hours (if available).

Reproductive toxicity. A robust summary for a 3-generation reproductive toxicity assay in rats exposed to C_{10}-C_{14} LAS, sodium saltan analog, in diet, was missing the CAS registry number for the test substance and details about the specific parameters that were evaluated.

Developmental toxicity. A robust summary for a developmental toxicity assay in rats exposed to Japan LAS was missing the CAS registry number, cation, and the purity of the test substance and details about the specific parameters that were evaluated (both maternal and fetal).

Ecological Effects

Study details were missing in all of the submitted summaries.

Fish. Missing study details included the following: test substance purity, number of fish per group, age and mean weight of the fish, test concentrations, use of appropriate controls, signs of toxicity, water quality characteristics (*e.g.*, hardness, pH, dissolved oxygen, alkalinity, and temperature), control response, statistical methods, and 95% confidence limits.

Invertebrates. Missing study details included the following: test substance purity, age and number of daphnia per group, test concentrations, use of appropriate controls, signs of toxicity, water quality characteristics (*e.g.*, hardness, pH, dissolved oxygen, alkalinity, and temperature), control response, statistical methods, and 95% confidence limits.

OECD 202 ("Acute Immobilization Test in Daphnia sp.") recommends that the pH of the controls and test solutions be measured at the beginning and the end of the test, and that the pH of the test solutions not be adjusted. It was not clear from the inadequate details in the summaries that these recommendations were followed.

Algae. Missing study details included the following: test substance purity, test concentrations, number of replicates per group, culturing apparatus, culture conditions (*e.g.*, lighting and temperature), use of appropriate controls, control response, statistical methods, and 95% confidence limits.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.